Declaration

I, Simon Philipp Hoerstrup, hereby declare and state:

THAT I am one of the authors and inventors of a prior art document DE 199 19 625 A1 to the US application 10/523.618;

THAT I am one of the inventors of the invention disclosed and claimed in the present US application 10/523.618;

THAT I have reviewed the outstanding Office Action from the US-Examiner dated July 9, 2010 in the above referenced application, especially the Examiner's comments with regard to the prior art document DE 199 19 625 A1 (Hoerstrup,

THAT I conclude that none of the cited prior art references, alone or in combination, teach or suggest my invention as set forth in the currently pending claims;

THAT, at least because the prior art does not have a teaching of a biodegradable carrier in combination with a poorly degradable frame, the claims should be found allowable.

1. My statement in DE 199 19 625 A1

The examiner states, in page 3 of the pending office action, that I, in DE 199 19 625 A1 anticipated the problem to stent a heart valve by the statement (quoted from the partial English translation of said document, submitted to the USPTO on April 2, 2010) *"This tissue is however useful for implantation into a human heart only in a limited manner, since, due to its weak mechanical properties, it would not be suitable for the flow conditions at the place of implantation."*

This problem cited in DE 199 19 625 A1 is solved by conditioning the implant to withstand the flow conditions at the place of implantation. I therefore respectfully disagree with the examiner's above mentioned statement. The purpose of my above statement in said application DE 199 19 625 A1 concerning my previous invention was to declare the object of my previous invention, which was to provide an improved homologous heart valve implant by submitting the tissue matrix to increasing flow rates in a pulsatile flow chamber, in order to condition the implant for the flow conditions present in the heart following dissolution of the carrier structure (see column 2 of the specification). My statement was not made to imply that it would be necessary to stent the implant and to provide an external support. On the contrary the meaning is that internally the tissue needs to be strengthened. Consequentially, a stent or

frame is not mentioned anywhere in my previous application DE 199 19 625 A1. My disputed statement is followed by a description of the formation of a flow-resistant connective tissue matrix by a slow adaptation of the flow rates in a pulsatile flow chamber, which is the core of my invention set forth in DE 199 19 625 A1. So the idea is not to provide external support but to internally strengthen the tissue.

To summarize the above, at the time of my previous invention, I did not disclose nor suggest anywhere in the corresponding application DE 199 19 625 A1 that an external support such as a frame would be necessary to increase the stability of the heart valve implant. Quite by contrast, I was aiming at providing heart valves with a greater inner stability by conditioning the tissue matrix in a pulsatile flow chamber. The conditioning provides a greater inner stability to the colonized support/valve structure in itself.

2. My present invention

The present invention of mine goes a step further, to even further improve the implant of DE 199 19 625: The passage on page 2, lines 24-30 of my present application cites DE 199 19 625 A1 and states: *"At the time of its implantation, the heart valve described in DE 199 19 625 almost entirely comprises autologous cell material, which is then sewn into the receiving heart. Under certain circumstances, one disadvantage of this heart valve could be that the surgical implantation is technically difficult to perform. There could moreover be a problem if the suture has to pass through the autologous, tissue-engineered tissue to be sewn in. because of the extremely high load the heart valve is subsequently exposed to in the human body, tears could occur in the region of the suture."*

The object of my present invention was therefore to provide improved homologous heart valves and a method for their production. Such heart valves have all the advantages of the heart valve known from DE 199 19 625 but show the improvements that they avoid a suture having to be passed through the connective tissue structures of the heart valve at the time of implantation of the valve. They can be produced by the methods according to the invention, withstand the flow conditions prevailing in the body and are easy to implant surgically.

Furthermore, fixing a conditioned valve structure having a biodegradable support into an external fixation such as a stent, as set forth by my present invention, offers double stability, an inner and exterior stability, to the implant.

The conditioned heart valve of my present invention contains a biodegradable support which begins to degrade at least 8 days post colonization and is completely degraded no later than 3 months after colonization, and a poorly degradable frame which does not degrade prior to a year after colonization. The differential degradation properties of the support and the frame first provide temporary stability of the implant in the body post-implantation, but then also allow a gradual development of a finally completely autologous implant over time without additional surgery, once the implant's tissue is strong enough on its own in the body, making the stability provided by the "foreign" material redundant.

My present invention offers the unexpectedly superior, experimentally verified result that the transplantation of the heart valve is greatly facilitated for a heart surgeon in comparison to a regular tissue-engineered heart valve such as e.g. according to my previous invention. Due to its greater overall stability, the new heart valve can be handled and set into place easier, and ingrowth is facilitated, as the new heart valve lies closer against the surrounding tissue due to its more consistent structure. This entails that, as could be shown experimentally, the risk for the need of re-operation after implantation (for instance due to insufficient adherence to surrounding tissue) is greatly reduced.

Neither DE 199 19 625 A1 (Hoerstrup), nor US 4,758,151 (Arru), alone or in combination, teach or suggest my invention as set forth in the currently pending claims. The combination of a biodegradable support and a poorly degradable frame, in further combination with flow-conditioning, is neither taught nor suggested therein.

I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true.

Zurich, 07.10.2010

Place, Date

Simon P. Hoerstrup